UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,318	11/09/2001	Maria G. Pallavicini	02307O-120900US	1486

20350 7590 08/25/2004

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,318	PALLAVICINI ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-16 are pending and under examination.

Claims 17-28 have been cancelled.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons advanced in the last Office action.

Response to Arguments

Applicants argue that the specification provides sufficient guidance both in the general discussions and examples with specific factors to consider. The specification teaches that the appropriate size of the subsequences inserted into a phage

display library can be determined based on the relative numbers of introns and exons, and that the appropriate size of the subsequences should ensure the library to have enough members to represent all or the vast majority of the genomic fragments to be analyzed (page 13, lines 25-31). Further discussions on the size restrictions relating to the gene structure, such as intron-exon pattern, size of the target region, stop codon frequency, exon size, etc. can be found, e.g., on page 14, line 12, to page 15, line 5. Moreover, the specification teaches how to determine the appropriate size of the subsequences by way of example. In Example 1 on page 30 and in Figure 1, the process of insert size selection for H11 P1 is described, which takes into consideration factors such as exon size, stop codon frequency, and resulting library size. Because the specification offers both generalized description and specific examples on how to choose the proper size of subsequences to be inserted into a phage display library, one of skill in the art would, upon reading this specification that the inventors had the claimed invention in their possession at the time this application was filed.

In response, as stated by applicants the specification provides a general description of the invention. The detailed description is drawn to very method steps, conditions and other

experimental factors for H11P1. Applicants recognized that while in ***theory***, it should be possible to clone all genes encoding proteins with affinity for another molecule. Factors such as the size of the binding domains, the folding of the polypeptide and also, in some cases, the requirement of a second domain or subunit may limit which proteins can be displayed on the phage surface in an active form. (Jacobson Biotechniques). The specification at page 32, states that even for the specific fragments, selection was made of the fragment sizes in order to maximize enrichment of exons. Selection of the target insert size range to maximize exon display was based upon in silico analyses of the size distribution of exons in genes within the H11 P1. Long fragments (>300 bp) are more likely to contain intron sequence with stop codons, which would prevent translation of displayed protein thereby reducing the diversity and complexity of the library. On the other hand, short fragments have a lower likelihood of folding into a domain structure, which could mimic the conformational epitopes that antibodies typically recognize. Thus, while longer fragments are better for domain structure, the potential problems with introns and stop codons suggests the need for an optimal bp. Because of the high unpredictability in the art and the huge genus cover by the claims, the single example is not adequate to

describe the huge genus of the claim. See the See University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003) for lack of written description and enabling disclosure. A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993).

Applicants admit that the claimed method may not successfully identify every exon in a eukaryotic genomic fragment. But argue this is irrelevant to the written description assessment but relevant to the enablement assessment. Applicants contend that even the enablement requirement does not require the claimed method to be operable for identifying every exon in a eukaryotic genomic fragment. The enablement requirement requires the specification to describe the claimed invention so as to allow one of skill in the art to make and use the invention. As stated in MPEP 2164.01(b), "as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable

correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." Applicants contend that the present specification describes a method that would allow the identification of at least some, if not most, exons from eukaryotic genomic fragments, which clearly bears a reasonable correlation to the entire scope of the claim. Thus, even if the Examiner is correct in that the claimed method may not be used to identify every exon in a eukaryotic genome, this factor alone is insufficient to support a written description or enablement rejection.

In reply, the correlation of the single example in the specification can hardly be considered a reasonable correlation of the huge claim genus. The high unpredictability in the gene art is so notoriously known, as evident from the statement of applicants, supra. Thus, it cannot be ascertained from the single example obtained from one gene its predictability to the numerous different eukaryotes (i.e., exon genes). The limited guidance or direction does not provide the ample description and enablement required for all or any types of exons for any eukaryotic genes.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fack (J. Of Immunogical Method) in view of Buckler et al (WO 92/13071) and further in view of Winter for reasons set forth in the last Office action.

Response to Arguments

Applicants acknowledge that the Fack et al reference describes a method for identifying antibody epitope using a gene-fragment phage display library, which expresses fragments of the coding sequence for a protein of interest (e.g., page 46, left column, section 3.1). But argue that Fack et al used a phage display library that expressed only fragments of the coding sequence of a protein; the library did not include any "noncoding subsequences." Neither is the inclusion of "noncoding

sequences" suggested anywhere in the reference. The Fack et al. reference therefore does not provide all claim limitations and cannot anticipate the pending claims.

In response, applicants' attention is drawn at page 45, 2.3, which relies on the methods described by Smith and Scott (1993). The details are given in the manual of cloning in vectors supplied with the expression kit by Smith. In it plasmid DNA was digested with DNase to obtain DNA-fragments of between 50 and 400 bp (i.e., the coding and non-coding fragments). See further page 49, Fig. 4 that shows the encoded protein (epitope) containing the non-encoded (non-epitope region). See also the Discussion section at page 50.

It is considered that the fragment of Fack contains implicitly or at least suggest said non-coding region since the binding occurs only in the coding (epitope) region. It is considered that the fragments of 50-160 contain a non-coding region since the total fragments code only for a specific epitope.

Applicants further argue the limitation of "noncoding subsequences" of the W092/13071 relates to a method for exon amplification. The Winter et al reference relates to recombinantly producing antibodies using phage display technology. Neither supplies, explicitly or implicitly, the

missing claim limitation of "noncoding subsequences." Thus, not all claim limitations are provided by the cited references.

In response, Buckler (WO92/13071) discloses at e.g., page 2, lines 13- 20 that the method of exon amplification is useful for fast and efficient isolation of a coding sequence from a complex mammalian genomic DNA. The isolation of the amplified exon would indicate its isolation from the non-coding region of the complex gDNA. See further page 7, lines 3-28; page 12, lines 1-30 and the Examples.

Winter is employed not for the purpose as argued. Rather for the advantage derived in the used of antibodies i.e., as potential reagents for research and therapy. Accordingly, the combined teachings of the prior art would lead one having ordinary skill in the art to the claimed method.

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened

statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571)272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
August 20, 2004